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Retrospective evaluation of unexpected events during collection of blood donations performed with and without sedation in cats (2010-2013).

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Review

1 **Abstract**

2 **Objectives** – To review the feline blood donor records from a single center and to compare blood
3 donations that were performed with and without sedation.

4 **Design** – Retrospective observational study from 2010 to 2013.

5 **Setting** – University teaching hospital.

6 **Animals** – Client-owned healthy cats enrolled in a blood donation program.

7 **Interventions** – None.

8 **Measurements and Main Results** – Blood donation was performed 115 times from 32 cats during the
9 study period. Seventy donation events were in unsedated cats and 45 donation events were in sedated
10 cats. For each donation the anticipated volume of blood to be collected, the actual volume of blood
11 collected, the sedation protocol if used, and any unexpected events (UEs) in the peri-donation period
12 were recorded. UEs were coded into 6 categories; movement during donation, donor anxiety,
13 inadequate blood volume obtained, jugular vessel-related UEs, additional sedation requirement, and
14 evidence of cardiovascular or respiratory distress. The Fisher’s exact test was used to compare the
15 frequency of UEs between sedated and unsedated donations. Unexpected events were recorded in 54
16 of 115 donations, with 61 donations having no UEs. In the donor population movement was reported as
17 an UE in 0% (0/45) cats that donated under sedation and 34.3% (24/70) cats that donated unsedated
18 (P<0.001). Donor anxiety was reported as an UE in 4.4% (2/45) of the sedated group and 20.0% (14/70)
19 of the unsedated group (P=0.014). Unsedated donation did not lead to an increased likelihood of
20 inadequate donation volume, jugular vessel-related UEs or cardiac or respiratory distress. In the sedated
21 group, 17.8% (8/45) donations required additional sedation.

22 **Conclusions** – Movement during donation and signs of donor anxiety were more frequently reported in
23 unsedated blood donations compared to sedated donations. However, these were considered minor

issues, to be expected in unsedated cats being gently restrained. Therefore unsedated feline blood donation for transfusion is a viable alternative to sedation or anaesthesia.

Abbreviations

UE – unexpected event

Introduction

Current recommendations for harvesting feline blood donations describe the use of general anesthesia or heavy sedation of the donor.^{1,2,3} As feline critical care has advanced the demand for blood products has increased, however availability of feline blood products has remained limited.³⁻⁵ Veterinarians have used client- or staff-owned cats or in-house colony cats as blood donors, purchased blood products from commercial blood banks or used hemoglobin-based oxygen-carrying solutions^a to aid medical management of cats with severe anemia.⁶ The purchase of packed red blood cells can be cost prohibitive and commercial feline blood banks are not available or feasible in many parts of the world. Moreover, hemoglobin-based oxygen carrying solutions are no longer available.⁷ Therefore, often on-demand feline donation is the preferred option for veterinarians. Sedation with recommended agents, including ketamine-midazolam combination or inhalational agents to facilitate blood donation, has been reported to lead to hypotension and death.⁸⁻¹⁰ Performing feline donations without sedation, as is standard practice for canine donation, may have a number of advantages including decreasing donor morbidity and mortality, thereby making the process more appealing to potential blood donor owners. To the best of the authors' knowledge, there are no previously published reports of feline blood donation without anesthesia or sedation in cats. The objectives of this retrospective study were to describe the unexpected events that occurred during blood donation in cats with and without sedation.

46

47 **Materials and Methods**

48 The institution’s blood transfusion log was searched to identify all feline blood donations that
49 occurred between December 2010 and December 2013. Each blood donor record, which details
50 objective data and subjective comments on the ease of the donation were reviewed for any UEs. Donor
51 age and bodyweight prior to each donation were recorded. The number of previous donations, volume
52 of blood expected, actual blood volume retrieved, any UEs encountered and the sedation protocol, if
53 utilised, were recorded for each donation. Cases were excluded if records were incomplete.

54 In accordance with our institution’s blood donor program protocols, cats recruited to be blood
55 donors were aged between 1 and 8 years of age, had normal body condition, were healthy with no
56 previous or on-going medical illnesses, were living in a household where no animal had international
57 travel and were current on recommended vaccinations, flea and intestinal worming treatments. At
58 induction into the blood donation program, donor cats had a complete blood count,^b a serum
59 biochemical analysis,^c *Mycoplasma haemofelis*,^d *Candidatus Mycoplasma haemominutum*^d and
60 *Candidatus Mycoplasma turicensis*^d polymerase chain reaction assays, qualitative Feline Leukaemia Virus
61 (FeLV) antigen^e and Feline Immunodeficiency Virus (FIV) antibody^e assessment and blood typing^f
62 performed. Prior to recruitment to the feline blood donation program, cats received a behavioural
63 assessment from the Transfusion Medicine Service nurse. For inclusion into the program, the cat must
64 be deemed to be tolerant of new surroundings, of handling and be tolerant for venipuncture (for
65 donation of blood samples to assess eligibility for enrolment onto the program) without marked manual
66 or any chemical restraint. Once enrolled, donor behaviour is monitored closely and donors are retired
67 from the program if they become intolerant of blood donation. It is also important to assess whether
68 the cat finds the procedure stressful.

Donations were performed either with or without sedation. Sedation was provided using 1 of 3 protocols.^g Additional sedation was administered if deemed necessary based on temperament of the cat during preparation for blood donation.^h Assessment as to whether sedation was required was made prior to each donation event. If the cat required more than gentle restraint during physical examination and blood sampling to check fitness to donate, sedation for the donation was administered. Both unsedated and sedated donors had an intravenous catheter placed into a cephalic vein. At a minimum of 45 minutes prior to cephalic catheter placement, **lidocaine 2.5%/prilocaine 2.5% creamⁱ was applied over the cephalic and jugular veins to decrease donor perception of intravenous catheter placement and venipuncture for blood donation, respectively.**

The procedure was performed with one phlebotomist and two patient care assistants. Donations were performed in a dedicated donation room, where donors were given time to acclimatise to their environment. The donor sits and generally only gentle restraint was used to hold the head upwards to allow access to the jugular vein where blood for donation is collected. In some cases forelimbs were also gently restrained. The Transfusion Medicine Service trained phlebotomist used a 19 or 21 gauge Terumo^j butterfly needle to perform venipuncture, allowing collection of the donation. The patient care assistant monitored behaviour, respiratory rate and demeanour. If the cat demonstrated excessive movement, the procedure was ceased or progressed to sedation. To allow this to be performed with minimal disruption, sedation was already prepared and a cephalic intravenous catheter was always in situ.

Duration of donation was identified as time from placement of cephalic catheter to initiation of intravenous fluids after donation event. Two investigators independently coded all the UEs noted in each blood donor record and grouped each event into 1 of 6 predetermined categories: movement during donation (recorded on the donation record), donor anxiety, inadequate blood volume obtained

(based on expected donation volume), jugular vessel-related UEs (including hematoma formation), additional sedation requirement, and evidence of cardiovascular or respiratory distress. Donor anxiety was classified in this study as vocalisation (eg, hissing, growling, yowling) and swiping. For the purposes of this study, movement was classified as any deemed noteworthy by the transfusion nurses including movement that necessitated either repeat jugular venipuncture or abortion of the donation. **The unexpected events were further grouped into two broad categories, major and minor. Major UEs were defined as any UE that endangered a cat or member of staff, with all other UEs being classified as minor.** If there was any difference in coding between the investigators, the case record was jointly reviewed and an agreement reached. A Fisher’s exact test was used to compare the frequency of each UE between the unsedated and sedated donation events using a commercial statistical software program^k for all statistical analyses.

Results

Donor characteristics

The median age of the donors that were bled unsedated was 5 years (range 1.0-8.0). The mean age of the donors that were bled sedated was 4.5 years (standard deviation 2.1). The mean weight of donors that were bled unsedated was 5.3 kilograms (standard deviation 0.8). The median weight of donors that were bled sedated was 4.9 kilograms (range 3.6-6.5).

Comparison of sedated and unsedated donors

One hundred and fifty eight blood donations were performed during the study period, including 89 unsedated and 69 sedated donations. Forty-three donations were excluded due to incomplete data,

of which 19 were unsedated and 24 sedated donations, leaving a total of 70 unsedated and 45 sedated donations included in the study.

Twenty cats had blood donations performed without sedation and 18 cats had blood donations performed under sedation. Of the cats that were bled without sedation, 6 cats donated once, 4 donated twice, 3 donated 3 times, 3 donated 5 times and 1 cat donated 7 times, 2 donated 8 times and 1 donated 9 times. Of the cats that were bled under sedation, 6 cats donated once, 3 cats donated twice, 4 cats donated 3 times, 4 cats donated 4 times and 1 cat donated 5 times. There were 6 cats that donated both with and without sedation.

Of the cats that were bled without sedation, 14 were first time donors and in the cats that were bled sedated, 14 cats were first time donors. First time donors comprised 24.3% of all donations, with inadequate blood volume retrieved (n=7), movement (n=6) and donor anxiety (n=6) being the most common UE in the first time donors, followed by additional sedation requirement (n=3), jugular vessel-related UEs (n=2) and evidence of cardiovascular or respiratory distress (n=1). Eleven first time donors had no UEs.

Five cats in total that were bled sedated were eliminated from the donor program; one due to owner request, one due to relocation and three for negative behaviour. Of the three donations where negative behaviour was displayed, stress was displayed prior to the defined donation period. We considered it normal behaviour for a cat to resent intravenous catheter placement. No cat that participated in an unsedated donation was eliminated from the donor program. Eight donations progressed from unsedated to a sedated.

The minimum, maximum and mean volumes of blood collected from sedated donation events were 6.7mL/kg, 11.8mL/kg and 9.7mL/kg, respectively. The minimum, maximum and mean volumes of

136 blood collected from the unsedated donation events were 5.6mL/kg, 12.4mL/kg and 9.2mL/kg,
137 respectively.

138 A total of 61 donations had no UEs reported (61/115, 53.0%), of which 28 (62.2% of all sedated
139 donations and 24.3% of all donations) were donors that were sedated and 33 (47.1% of unsedated
140 donations and 28.7% of all donations) that were donors that were not sedated. No major UEs were
141 noted in either sedated or unsedated cats.

142 There was a statistically significant difference between frequency of UEs in the donation events
143 where the cats were sedated for donation and the donation events where the cats were unsedated for
144 both movement ($P<0.001$) and donor anxiety ($P=0.025$). In the donation events where the cats were
145 sedated for donation, 0/45 had movement reported as an UE, whereas in the donation events where
146 the cats were unsedated for donation, 24/70 (34.3%) cats moved during donation. In the donation
147 events where the cats were sedated, 2/45 (4.4%) had donor anxiety reported as an UE, whereas in the
148 donation events where the cats were unsedated, 14/70 (20.0%) had donor anxiety as a UE. Of the cats
149 that were sedated for donation, 8/45 (17.8%) required additional sedation.

150 **No statistically significant difference was detected** between the frequency of inadequate
151 volume retrieved ($P=1.000$), jugular vessel-related UEs ($P=0.244$), cardiovascular/respiratory UEs
152 ($P=0.279$) and donations with no unexpected events ($P=0.129$) when comparing the sedated and
153 unsedated cats (Table 1).

154 Cardiovascular or respiratory distress was seen in 3 cats in this study population, all of which
155 were cats that donated blood without sedation. One of these cats was noted to have panted post-
156 donation and also had a gallop prior to the subsequent blood donation. This cat went on to perform 2
157 subsequent donations without a UE observed and was then retired due to age. This cat had no
158 echocardiogram performed at any point. A second cat that had tachypnea post donation was noted to
159 have an intermittent and rate-dependant heart murmur and gallop rhythm prior to donation (no

echocardiogram was performed) and this cat had another 2 subsequent uneventful donations after this UE and was then retired due to international travel. The final cat had already donated 5 times where 2 were uneventful and for 3 he displayed donor anxiety and then he had the documented UE of collapse, vocalisation, panting and defecation. This cat had a normal echocardiogram performed by a board certified cardiologist.

Discussion

Feline blood donation has been previously described in sedated or anesthetized cats.^{1,2} The procedure by which blood is collected from an unsedated donor is similar to that for a sedated donor, however there is a greater emphasis placed on donor behavior and temperament when considering donor selection.^{11,12} Donors must be tolerant of handling and not fearful of new people or surroundings. These characteristics make an ideal blood donor, be it for unsedated or sedated donation, however, if for use in an unsedated donation, the cat must be able to tolerate gentle restraint for an extended period of time (approximately 10 minutes).

Recruitment of client-owned cats to participate in a feline blood donor program can be difficult, and the Transfusion Medicine Service at the authors' hospital aims to decrease the risk to the donor and to increase the appeal of the process to potential new feline blood-donor owners. Maintenance of the blood donor population via recruitment of owned cats is vital to the blood donor program, as the author's institution has no access to commercial feline blood banks.

Sedation or anesthesia carries a risk of adverse effects including hypotension, hypoxemia, decreased renal perfusion and death. These consequences make the use of anesthetic agents to chemically restrain the blood donor less appealing. Pharmaceutical agents used for chemical restraint of cats in this transfusion program have been described previously.³ Several veterinary studies have

described the effect of sedation on feline blood donors. Killos et al, assessed the effects of the use of 2 anesthetic protocols cats used for blood donation and found that 84% cats anesthetized with sevoflurane and 42% of cats anesthetized with ketamine/midazolam/butorphanol combination developed hypotension that required treatment with fluid therapy and cats in the ketamine/midazolam/butorphanol group also suffered hyperthermia and their owners noted a slower return to normal behavior.⁸ Iazbik et al studied feline blood donors anesthetized with sevoflurane and found that their heart rate and blood pressure decreased significantly post donation and noted that although blood pressure and heart rate decreased, there were no adverse effects secondary to donation seen (defined as a lack of weakness, pallor or collapse after recovery from anaesthesia).⁹ A final study used zolazepam and tiletamine in blood donors and found that rectal temperature significantly decreased and blood pressure significantly increased post donation but there was no evidence of pallor or collapse after recovery from sedation.¹³ Although the cardiovascular effects seen in these studies appear minor, they are present and the risk of adverse effects (some of which may not have been detected in these studies) and death is present.

Two studies above, Killos and Iazbik discuss the effects of feline donation under sedation or anesthesia on blood pressure, heart rate, packed cell volume and mucous membrane pallor.^{8,9} However, other potential adverse events such as jugular vessel hematoma are not discussed. In human medicine, adverse events occur in approximately 4-36% of blood donations.^{14,15} Environmental factors are documented to play a major role in the frequency of human donor adverse events, with an increase in events in crowded conditions, heat, increased noise and with extended waits prior to donation. The most common adverse events in people include weakness, sweating and pallor.¹⁴ One cat in this study collapsed post donation which could be described as weakness (no cause was found for the collapse and the cat rapidly recovered), but otherwise these adverse events described in humans were not observed in the current study of feline blood donors. Although weakness should have been noted, cats do not

sweat and pallor may not have been noted on the record as an unexpected event. Less frequently, cardiovascular unexpected events are seen in human blood donors, such as hypertension, hypotension, bradycardia and dizziness. These are presumed to be the result of a vasovagal reaction rather than true cardiovascular compromise.¹⁴

Venipuncture-related adverse events (e.g., hematoma, nerve injury, local infection and thrombophlebitis) are common in human blood donors with a phlebotomy-related reaction rate of 9-36%, with a higher incidence in autologous donors due to underlying medical conditions.^{14,15} A similar value of vessel related adverse events was seen in this study (11% of cats), with the level not being significantly different between unsedated (n=10, 14.3%) and sedated donors (n=3, 6.7%). This study has found that unsedated feline blood donation did not lead to an increased likelihood of jugular-vessel related unexpected events, such as hematoma formation when compared to donation in the sedated feline donor.

Cardiovascular or respiratory distress was not more frequent in cats that donated unsedated when compared to cats that donated sedated in this study. No cats that donated sedated had a cardiovascular or respiratory UE. Three cats that donated unsedated did have a cardiovascular or respiratory UE. In each case a physical examination was performed by a veterinary surgeon within minutes of the UE and they were found to be normotensive. The respiratory signs included tachypnea and panting and the collapse was presumed to be cardiovascular in origin. Of the two respiratory UEs, one involved a donor that had an intermittent gallop and the other involved a donor with an intermittent murmur and an intermittent gallop. Both of these cats had donations with no UE after these events. The cat that collapsed had previously had a normal echocardiogram and after this UE had multiple other donations with variable UEs, including donor anxiety and movement. The cause of the distress seen is difficult to assess in a retrospective study, however, the 2 cats with a respiratory UE (minor episodes of panting) were likely stress related and the cat with an episode of collapse may have

231 had vasovagal syncope.¹⁵ In retrospect, consideration should have been made to retire all 3 cats from
232 the program after these events.

233 It is interesting to note that in a 1999 study of adverse events in human blood donors by
234 Trouern-Trend et al first time donors were 5 times more likely to have a vasovagal reaction involving
235 syncope than repeat donors.¹⁶ First time donors in this study were not more likely to have an UE than
236 veteran donors.

237 In the current study, movement during donation and signs of donor anxiety were significantly
238 more frequently reported in unsedated blood donations compared to blood donations performed under
239 sedation. Movement during donation was the most frequent UE occurring in a third of the unsedated
240 donations. Minimization of this UE should be achieved with appropriate donor selection, however, with
241 skilled phlebotomists and handlers, the effect of minor donor movement on successful donation is
242 minimal. Donor anxiety was reported in one fifth of unsedated feline donors. This included donor
243 behavior that may be interpreted as stress including vocalization and aggression. This behavior is
244 important to record to determine the viability of a donor for future donations. Both donor movement
245 and donor anxiety were significantly more likely to occur in the unsedated donations, which is to be
246 expected as appropriate sedation would prevent movement. Two sedated donations did have donor
247 anxiety noted as an UE. These occurred in 2 separate cats, which exhibited growling and hissing during
248 handling and were aggressive after donation. Both cats were retired from the donor program. Of the 14
249 donation events in the unsedated group that were noted to have donor anxiety, 6 were vocal alone
250 (e.g., hissing, growling), 3 were noted as subjectively appearing anxious or scared, 2 resisted handling
251 and one exhibited marked aggression. Donor anxiety often leads to exclusion from the unsedated
252 program or progression to full sedation during the donation and assessment for inclusion or exclusion to
253 the donor program is based upon transfusion team assessment.^{11,12}

The results of this study suggest that the impact of both movement and donor anxiety on donation success is not marked as there was no significant difference between sedated donations and unsedated donations when considering vessel related complications or inadequate donation volume obtained. Retrieval of the desired blood volume must be ensured to make the donation of feline blood in the unsedated cat a viable procedure, for owner, transfusion service and recipient. The movement and signs of donor anxiety were considered minor issues, to be expected in unsedated cats being gently restrained and were not noted in the sedated group as they should not be seen in an appropriately sedated cat.

There were several limitations to this study. Primarily, this study relied on accurate, complete and consistent recording of blood donation by staff at the time of donations. The majority of the donations were performed by 3 transfusion medicine nurses, leading to fair consistency in recording of events. The relevance of the unexpected event of movement noted in the study to donation practice is difficult to gauge. It is possible recording of movement in the records was zealous as unsedated blood donations was a newly instituted protocol and monitoring of this protocol was used to determine the feasibility of unsedated blood donations. Measurements of heart rate, respiratory rate and blood pressure were not regularly recorded post donation to minimise handling of the patient to reduce donor anxiety, and were only performed when a patient showed clinical signs that indicated a cause for concern. Therefore, there may have been a higher incidence of cardiovascular and respiratory unexpected events than was recorded.

Additionally, the population of the study was not uniform, as many cats had performed a number of donations prior to inclusion in this study population. In humans, up to 50% of the donor population are reported to be repeated donors as compared to reports of 35% of repeated donors in dogs.⁶ A blood donor may become more or less compliant as they perform repeated donations.

In conclusion, this study describes the process of unsedated feline blood donation and the ease with which it can be performed. The appeal of unsedated blood donation is high due to increasing demand for feline blood products leading to the pressure to increase the number of donor recruits in a transfusion program. Although the rate of movement and donor anxiety unexpected events were significantly higher in the unsedated donations, the effect of this on donation success was minimal and in the majority of cases they were not felt to be severe enough to prevent continuation as an unsedated blood donor. As the donor anxiety was minimal and there was no negative impact on vessel related complications or volume retrieved, the appeal to perform feline blood donation in the unsedated blood donor is high. The use of unsedated feline blood donors may also increase the appeal of blood donations to cat owners improving blood donor recruitment. As such unsedated blood donation for feline blood donation is a viable alternative to donation in the sedated or fully anesthetized cats.

Footnotes

a Oxyglobin, OPK Biotech LLC. Cambridge, MA, USA.

b (complete blood count), Advia 2120i, Siemens Healthcare Diagnostics Ltd. Camberley, Surrey, UK.

c (serum biochemical analysis), IL600, Instrumentation Laboratory. Birchwood, Warrington Cheshire, UK.

d *Mycoplasma haemofelis*, *Candidatus Mycoplasma haemominutum* and *Candidatus Mycoplasma turicensis* polymerase chain reaction assays, Langford. Bristol, Bristol, UK.

e Feline Leukaemia Virus (FeLV) antigen and Feline Immunodeficiency Virus (FIV) antibody assays, Westernblot ELISA, [MegaCor Diagnostik](#). Hoerbranz, Austria.

f Feline blood typing, Quicktest A+B, Alvedia via Pet Blood Bank Services Ltd. [Loughborough, Leicestershire, UK](#)

g Protocol 1 - Midazolam 0.2mg/kg & Ketamine 3mg/kg IV, Protocol 2 - Midazolam 0.25mg/kg &
Ketamine 5mg/kg IM, Protocol 3 - Midazolam 0.2mg/kg & Ketamine 3mg/kg & Butorphanol 0.2mg/kg IV.
h Midazolam 0.2mg/kg IV or Butorphanol 0.2mg/kg IV.
i Emla Cream 5%, APP Pharmaceuticals. Lake Zurich, Illinois, USA.
j Terumo syringe, Terumo Europe. Leuven, Belgium.
k Statistical Package for the Social Sciences (SPSS), IBM Corporation. Armonk, New York, USA.

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Table 1**Frequency of unexpected events in unsedated and sedated collections**

Unexpected event	Sedated donor group (n=45)	Unsedated donor group (n=70)
Movement during donation*	0 (0%)	24 (34.3%)
Donor anxiety*	2 (4.4%)	14 (20.0%)
Inadequate blood volume obtained	9 (20.0%)	15 (21.4%)
Jugular vessel-related (including hematoma formation)	3 (6.7%)	10 (14.3%)
Additional sedation requirement	8 (17.8%)	n/a
Evidence of cardiovascular or respiratory distress	0 (0%)	3 (4.3%)